REMARKS

I. Status of the Application

This is a response to the Office Action mailed on December 28, 2007. Claims 1-33 and 52-69 are now pending. Claims 18 and 19 were previously withdrawn. Claims 1, 5, 10, 16, 17, 29-31, 33, 52, 53, 59-61, 63-64, and 69 are amended herein. Claims 34 and 35 have been cancelled. The specification has been amended to correct typographical errors. Support for the amendments can be found throughout the specification and claims as originally filed. No new matter is presented by way of the amendments.

II. Reaffirmation of the Election of Species

Applicant affirms the election of omeprazole as the acid labile proton pump inhibitor, and sodium bicarbonate as the buffering agent. Claims 1-17, 20-35 and 52-69 fall within this election. Once patentability has been established for the elected species, Applicant may seek rejoinder of the non-elected species into the allowed claim set. Applicant also reserves the right pursuant to 35 U.S.C. §121 to file one or more continuation applications, including divisional applications, directed to the non-elected inventions.

III. Obviousness-Type Double Patenting

Claims 1-17, 20-35 and 52-69 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11, 13-39, 41, 44, 45 and 47-63 of copending Application No. 10/938,766; claims 44-85 of copending Application No. 10/893,092; claims 1-35 of copending Application No. 11/107,349; claims 1-15, 17, 18, 20-25, 54, 56-86 of copending Application No. 10/893,203; claims 48-58 of copending Application No. 11/138,763; and claims 1-55 of copending application No. 10/982,369. Without conceding to the appropriateness of this rejection, Applicant will submit a terminal disclaimer once allowable subject matter is indicated if necessary at that time.

IV. Dependency of Claims 52 and 53

Claims 52 and 53 are objected to as being of improper dependent form. Claims 52 and 53 have been amended to depend from the method of claim 1. Therefore, applicant respectfully

submits that these objections have been obviated and withdrawal of these objections is requested.

V. Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-17, 20-35 and 52-69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

First, the Office Action rejected claims 1, 5, 29-31 and 34 as indefinite because the phrase "at least some of the proton inhibitor" does not adequately define the bounds of the claims. Applicant respectfully submits that this rejection is now moot in light of the amendments made to claims 1, 5, 29-31 and 34. Thus, withdrawal of this rejection is respectfully requested.

Second, the Office Action rejected claim 32 as indefinite for defining a parietal cell activator as an excipient. It is respectfully noted that claim 32 does not recite excipients or parietal cell activators. Applicants assume that the Office intended to reject claim 33. Accordingly, claim 33 has been amended to delete parietal cell activator from the group of excipients. Applicant respectfully submits that this rejection has been obviated by the amendments presented herein and withdrawal of this rejection is respectfully requested.

Third, the Office Action rejected claims 1, 5, 29-31 and 34 as indefinite because the T_{max} and C_{max} parameters claimed did not specify the compound being measured. Applicant respectfully submits that this rejection has been obviated by the amendments made to claims 1, 5, 29-31 and 34. Thus, withdrawal of this rejection is respectfully requested.

Fourth, the Office Action rejected claims 57-59 and 62-67 as indefinite for lack of antecedent basis in claim 1. Applicant respectfully submits that this rejection has been obviated by the amendments made to claim 1. Thus, withdrawal of this rejection is respectfully requested.

VI. Rejections Under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 16 and 17 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner rejected the use of the term "prodrug" in these claims. Without admitting or conceding in any manner that rejected claims 16 and 17 fail to comply with 35 U.S.C. § 112, first paragraph and solely to expedite the prosecution of the present application, claims 16 and 17 have been amended to exclude the "prodrug."

Applicant respectfully submits that in light of these amendments, this rejection is now moot. Withdrawal of the rejection of claims 16 and 17 under 35 U.S.C. § 112, first paragraph is respectfully requested.

Claim 52 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement and the best mode requirement. Specifically, the Examiner rejected the use of the term "at risk of having" in these claims. Claim 52 has been amended to remove the term "or at risk of having." Applicant respectfully submits that in light of this amendment, this rejection is now moot. Withdrawal of the rejection of claim 52 under 35 U.S.C. § 112, first paragraph is respectfully requested.

VII. Rejections Under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 1-17, 20-35 and 52-69 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicant respectfully traverses this rejection.

Claims should be read in light of one of skill in the art. All that is necessary for enablement is that one of skill in the art be able to make and use the claimed invention using the application as a guide. The evidence provided by the applicant need not be conclusive but merely convincing to one skilled in the art. M.P.E.P. § 2164.05.

A. The specification discloses the prevention of GERD

The Office Action suggests that the claimed method is not enabled in so far as it relates to the prevention of GERD:

> The claims are directed to the prevention or treatment of GERD symptoms comprising administering an acid labile proton pump inhibitor (a) and a buffering agent (b). The Specification does not reasonably provide enablement for the methods of prevention within the full scope of the claimed compounds.

Office Action at Page 6. The Examiner also suggests that the claimed prevention modality is not enabled:

> The instant Specification is drawn to a showing of the pharmacokinetics and pharmacodynamics of omeprazole/sodium bicarbonate compositions (pages 69-89). These showings are clearly not predictive for prevention of GERD. The skilled artisan would not reasonably expect that the

> claimed pharmaceutical combination composition could be used to prevent GERD.
>
> There are no working examples drawn to a prevention modality in which the claimed pharmaceutical combination compositions comprising both an acid labile proton pump inhibitor (a) and a buffering agent (b) is shown to be clinically effective for prevention of GERD.

Office Action at Page 8. Applicant respectfully requests that this rejection be withdrawn in light of the following arguments and the current amendments, made without admitting or conceding in any manner that the rejected claims fail to comply with 35 U.S.C. § 112, first paragraph and solely to expedite the prosecution of the present application.

The term "prevent" or "prevention" as relates to a gastrointestinal disorder or disease, has been defined in the specification. The term, as defined, "means no gastrointestinal disorder or disease development if none had occurred, or no further gastrointestinal disorder or disease development if there had already been development of the gastrointestinal disorder or disease. Also considered is the ability of one to prevent some or all of the symptoms associated with the gastrointestinal disorder or disease." Specification at page 27, line 7. The words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. M.P.E.P. § 2111.01. Additionally, where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim. M.P.E.P. § 2111.01.

Again, the pending claims under examination are directed to methods of treating or preventing GERD symptoms and increasing gastric pH after a meal by administering compositions comprising a PPI and buffering agent prior to a meal. Applicant notes that the specification as submitted contains examples that would enable one of skill in the art to make and use the invention, given the level of knowledge in the art. For example, Applicant respectfully submits that the results of Trail Protocol SAN-15-CO1B, described in Example 8 and Fig. 13, disclose the administration of omeprazole (40 mg)-sodium bicarbonate composition within one hour prior to a meal results in prevention of GERD after the meal (p. 87, lines 7-19).

B. The specification discloses compositions providing the claimed pharmacokinetic and pharmacodynamic properties

The Office Action states on page 6, "the Specification fails to provide support for

attaining the gastric pH values pre and post meal as recited in Claims 1-3, 6-10 and 34 or proton pump inhibitor blood serum concentrations and time to maximum concentration recited in Claims 20, 21 and 57-69." Applicant respectfully requests that this rejection be withdrawn in light of the following arguments and the current amendments, made without admitting or conceding in any manner that the rejected claims fail to comply with 35 U.S.C. § 112, first paragraph and solely to expedite the prosecution of the present application.

The currently amended claims under examination are directed to methods of treating or preventing GERD symptoms and increasing gastric pH after a meal by administering compositions comprising a PPI and buffering agent prior to a meal. The specification as filed provides ample guidance to skilled artisans to practice the claimed inventions. For example, Applicants respectfully submit that the results of Trail Protocol SAN-15-CO1B, described in Example 8 and Figure 13, disclose that the administration of omeprazole (40 mg)-sodium bicarbonate composition within one hour prior to a meal results in prevention of GERD for at least one hour after the meal. The results from this study provide enablement to claims 1, 2, 6, 9 and 10. Further, the data presented in Figure 18A provide enablement to claims 3 and 34. Claims 7 and 8 have been cancelled.

With respect to the proton pump inhibitor blood serum concentrations and time parameters claimed in Claims 20, 21 and 57-69, Applicants respectfully submit that the data presented in Figures 2, 11 and 16, taken together with the results of Trial Protocol SAN-15-CO1B (described in Example 8 and Figure 13), provide enablement of Claims 20, 21, 57-63, 65, 66 and 69. Example 9 and Figure 17 taken together with the results of Trial Protocol SAN-15-CO1B (described in Example 8 and Figure 13), provide enablement of Claim 68. Claims 64 and 67 have been cancelled.

In light of the claims as currently amended and the arguments set forth above, Applicants submit that the scope of the claims is enabled. Applicants respectfully request that this rejection be withdrawn.

IIX. Rejections Under 35 U.S.C. § 102(a)

A. U.S. 6,489,346

Claims 1-17, 20-28, 30, 32-35 and 52-69 are rejected under 35 U.S.C. § 102(a) as being

anticipated by U.S. Patent No. 6,489,346 (Phillips, "the '346 patent"). In particular, the Office alleges:

> Phillips teaches a pharmaceutical compositions comprising a non-enteric coated proton pump inhibitor, in an amount of approximately 5 mg to approximately 300 mg, and at least one buffering agent, in an amount of approximately 0.1 mEq to approximately 2.5 mEq per mg of proton pump inhibitor. ... Furthermore, Phillips teaches methods of treating gastrointestinal conditions, including GERD, by administration of the proton pump inhibitor/buffer formulations described above (including omeptraozle/sodium bicarbonate).

Office Action at Pages 11-12 (internal citations omitted). Applicants traverse this rejection.

Applicants respectfully remind the Office that as set forth in the M.P.E.P., "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." M.P.E.P. § 2131 (citation omitted). Applicants respectfully point out that the Office fails to point to any disclosure in the '346 patent wherein administration of a composition set forth in the claims presented herein is administered for the treatment of GERD prior to a meal, as is required by the claims herein. Specifically, the Office's attention is directed to claim 1 which requires administration of the composition described therein within about 60 minutes prior to a meal. The Office's attention is also directed to Figure 14, which illustrates that Applicants have discovered a method of effectively controlling gastric acidity is achieved pre-meal, e.g., within 60 minutes of the meal. Applicants submit that the '346 patent does not expressly or inherently disclose the limitations of the pending claims, which require administering at least one acid labile proton pump inhibitor and at least one buffering agent so as to maintain gastric pH greater than about 4.0 for at least about 1 hour following the meal as claimed herein because it does not disclose administration of the composition prior to the meal. Therefore, the methods are distinct.

For at least the foregoing reasons, Applicants respectfully submit that the anticipation rejection of the pending claims over the '346 patent is improper because the '346 patent does not expressly disclose each and every element of the claim and the inherent disclose of the '346 patent does not remedy these defects. Accordingly, Applicants request that the rejection be withdrawn.

B. U.S. 2003/0191159

Claims 1-17, 20-35 and 52-69 are rejected under 35 U.S.C. § 102(a) as being anticipated by U.S. Patent Application No. 2003/0191159 (Phillips, "the '159 application"). Specifically, the Office alleges:

> Phillips teaches methods and compositions for treating gastric acid disorders, including *inter alia* GERD and heartburn, employing pharmaceutical compositions comprising an acid labile proton pump inhibitor and a buffering agent. ... The Phillips reference teaches that the composition buffering agent is present in an amount sufficient to increase gastric fluid pH of the stomach to a pH that inhibits acid degradation of the proton pump inhibiting agent in the gastric fluid, so as to allow absorption of the proton pump inhibiting agent and to provide a therapeutically effective serum concentration of the proton pump inhibitor of at least 150 ng/ml within 15 minutes after ingestion of the composition. Phillips further teaches a plethora of additional pharmacokinetic and pharmacodynamic information on proton pump inhibitor/buffering agent compositions. One of skill in the art would recognize that the pharmacokinetic and pharmacodynamic characteristics of a composition are complex and depend upon *inter alia* the age, body weight, general health, and sex of the patient, the rate of excretion, the drug combination and formulation, and the route of administration.

Office Action at Pages 13-14 (internal citations omitted). Applicants traverse this rejection.

Again, Applicants remind the Office that as set forth in the M.P.E.P., "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." M.P.E.P. § 2131 (citation omitted). Applicants respectfully point out that the Office fails to point to any disclosure in the '159 application wherein administration of a composition set forth in the claims presented herein is administered for the treatment of GERD prior to a meal, as is required by the claims herein. Specifically, the Office's attention is directed to claim 1 which requires administration of the composition described therein within about 60 minutes prior to a meal. Applicants submit that the '159 application does not expressly or inherently disclose the claimed methods, which require administering at least one acid labile proton pump inhibitor and at least one buffering agent prior to a meal so as to maintain gastric pH greater than about 4.0 for at least about 1 hour following the meal because it does not disclose administration of the composition prior to the meal. Therefore, the methods claimed herein are distinct.

For at least the foregoing reasons, Applicants submit that the anticipation rejection of the

pending claims over the '159 application is improper because the '159 application does not expressly disclose each and every element of the claim and the inherent disclose of the '159 application does not remedy these defects. Accordingly, Applicants respectfully request that the rejection be withdrawn.

IX. Rejections Under 35 U.S.C. § 103(a)

Claims 1-17, 20-35, and 52-69 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,489,346 ("the '346 patent") and over U.S. Patent Application No. 2003/0191159 ("the '159 application").

As discussed above, neither the '346 patent nor the '159 application disclose, suggest or teach the administration of a composition as set forth in the instant claims, i.e., prior to the consumption of a meal, particularly within about 60 minutes prior to a meal. Similarly, neither reference discloses, teaches, or suggests a method wherein the maintenance of a gastric pH of greater than about 4.0 for at least about 1 hour following the meal. The Office fails to address these limitations. As such, Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness.

Citing *In re Aller*, the Office apparently attempts to at least remedy the defect related to the gastric pH obtained while practicing a process claimed herein by submitting that the gastric pH parameters claimed would have been obvious to optimize. The Office states, "The determination of the optimum dosages, particle sizes, gastric fluid pH ranges, serum concentrations over time and drug release rates to employ or to seek with the presently claimed agents, would have been a matter well within the purview of one of ordinary skill in the art." *Office Action, page 16.* The Office's attention is directed to section 2144.05(II)(A) of the M.P.E.P., which discusses *In re Aller* and states:

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be

> *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.)

Thus, in *In re Aller*, the optimization was optimization of the process itself, not the result of the process. The gastric pH recited in the pending claims is obtained as a result of practicing a process claimed herein; it is not a parameter of the process that can be varied while practicing the process as was the case in *In re Aller*. Accordingly, the allegation that optimization of gastric pH is within the skill of the art is improper.

For at least the foregoing reasons, Applicants respectfully submit that the obviousness rejection of the pending claims over the '346 patent and/or the '159 application is improper. Accordingly, Applicants respectfully request that the rejection be withdrawn.

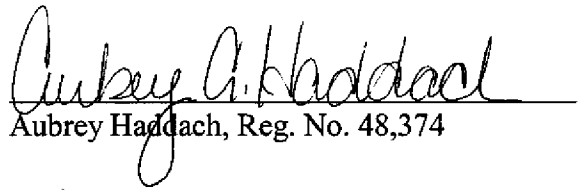
CONCLUSION

Applicant submits that this response fully addresses the Office Action mailed December 28, 2007. Applicants believe that for the reasons set forth herein, claims 1-17, 20-33, and 52-69 are in condition for allowance.

Should the Examiner have any questions, the Examiner is encouraged to contact the undersigned attorney at (858) 350-2319.

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI



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